115. Novel Approach to the Synthesis of 6-Substituted 5,6-Dihydro-2(2*H*)-pyranones

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Dedicated to Professor *George Büchi* on the occassion of his 60th birthday

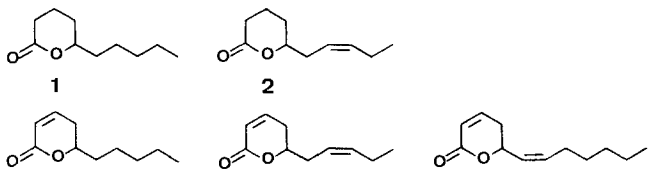
(11.V.81)

Summary

Easily accessible dihydropyrans **9**, **10**, **12** and **19** are precursors for the synthesis of 6-substituted 5,6-dihydro-2(2*H*)-pyranones and 6-substituted tetrahydro-2-pyranones. Syntheses of massoia lactone (**3**), argentilactone (**5**), tuberolactone (**4**) and jasmine lactone (**2**) from acrolein (**6**), acrolein dimer (**7**) or glutaraldehyde (**16**) are described.

Introduction. – Saturated and unsaturated aliphatic δ-lactones occur in several food flavors and essential oils [1] as the metabolites of higher molecular weight unsaturated fatty acids. Owing to their specific odor impression and low threshold concentration they play an important role as flavoring materials, and therefore practical syntheses of these δ-lactones are greatly demanded.

Whereas 5-decanolide (**1**) as well as its homologs are readily accessible from the *Baeyer-Villiger* reaction of the corresponding 2-substituted cyclopentanones, this approach is cumbersome for lactones containing C,C-double bonds (*cf.* syntheses of jasmine lactone (=(7*Z*)-7-decen-2-olide; **2**) [2]). Despite the relatively simple structure of 6-substituted 5,6-dihydro-2(2*H*)-pyranones, only a few syntheses to selected lactones are known [3]. We therefore looked for a general synthetic approach to (±)-massoia lactone (=2-decen-5-olide; **3**), (±)-tuberolactone (=(7*Z*)-2,7-decadien-5-olide; **4**), and (±)-argentilactone (=(6*Z*)-2,6-dodecadien-5-olide; **5**). The latter lactone **5** was isolated recently from the rhizomes of *Aristolochia argentina* [4], and its synthesis has not yet been reported.



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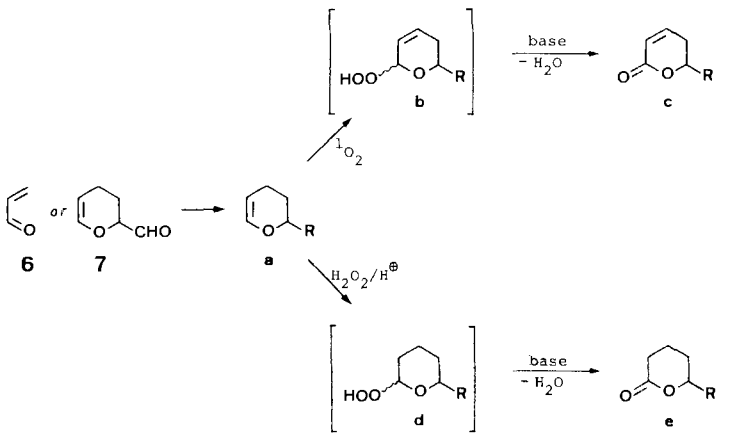
Our strategy consisted in constructing an appropriately 2-substituted 3,4-dihydro-2*H*-pyran of type **a** from acrolein (**6**) or acrolein dimer (**7**) followed by dye-sensitized photooxygenation and dehydration of the intermediate allylic hydroperoxide **b** to give lactone **c** *(Scheme 1)*[1]). This publication reports the application of this scheme to the syntheses of the lactones **3**–**5**. The dihydropyrans **a** are also ideal precursors for the construction of saturated δ-lactones **e** *via* acid-catalyzed

Scheme 1

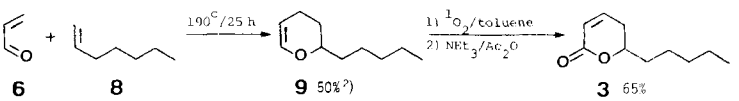


addition of hydrogen peroxide followed by dehydration [6] of the hydroperoxide **d**. This sequence is illustrated by a synthesis of jasmine lactone (**2**).

Results. – *Two-step synthesis of massoia lactone* (**3**) [3a] [3b]. Thermal [4+2]-cycloaddition of acrolein (**6**) and 1-heptene (**8**) gave regioselectively 2-pentyl-3,4-dihydro-2*H*-pyran (**9**) in 50% yield[2]) *(Scheme 2)*[3])[4]). Photooxygenation of **9** in toluene, using *meso*-tetraphenylporphine (= 5, 10, 15, 20-tetraphenylporphin) as sensitizer, and subsequent dehydration of the resulting allylic hydroperoxide afforded **3** in 65% yield.

Two-step synthesis of argentilactone (**5**) [4]. The required precursor 2-((*Z*)-1-heptenyl)-3,4-dihydro-2*H*-pyran (**10**) was obtained by a *Wittig* reaction of acrolein

Scheme 2



[1]) *Bartlett et al.* [5] studied the course of the photooxygenation of unfunctionalized 3,4-dihydro-2*H*-pyrans. Allylic hydroperoxides or dioxetanes are formed in variable ratios, depending on the enol ether structure and the solvent polarity.

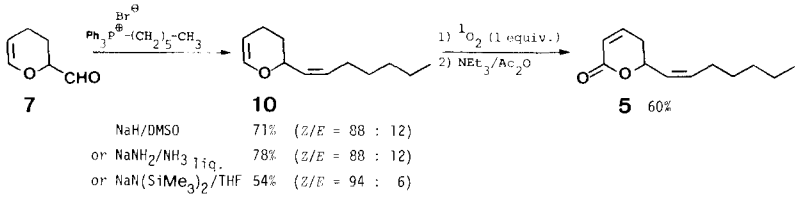
[2]) Based on consumed 1-heptene (**8**), conversion 32%.

[3]) For an attempted cycloaddition of acrolein and 1-hexene see [7].

[4]) No regioisomers of **9** were detected.

dimer (7)[5]) and hexylidenetriphenylphosphorane *(Scheme 3)*. Three sets of experimental conditions were studied: NaH/DMSO [8], $NaNH_2/NH_3$ (salt-free conditions) [9] and $NaN(SiMe_3)_2$ in THF [10]. The last method gave the highest stereoselectivity in favour of the (*Z*)-isomer. Argentilactone (**5**) was prepared from dihydropyran **10** with one equivalent of $^1O_2$ as above (s. synthesis of **3**). Interestingly, the C,C-double bond of the side chain was not affected by $^1O_2$.

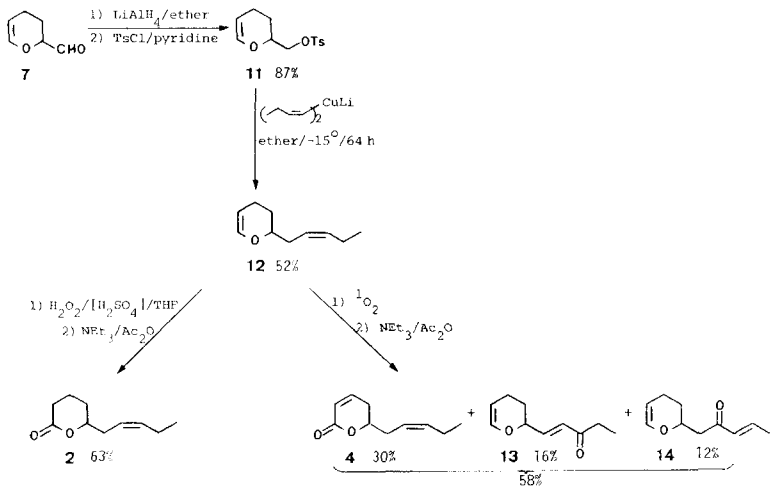
Scheme 3



Synthesis of tuberolactone (**4**) [3c] [3d] *and jasmine lactone* (**2**) [3c] [3d] [3e]. Acrolein dimer (**7**) was reduced, and the resulting alcohol was converted to its *p*-toluenesulfonate **11** in 87% overall yield (s. *Scheme 4*). For a highly stereospecific construction of the side chain, the lithium di((*Z*)-1-butenyl)cuprate was alkylated with **11** to afford dihydropyran **12** in 52% yield [11]. Photooxygenation and dehydration of the resulting hydroperoxide led to **4** (30%). In addition, two secondary products **13** (16%) and **14** (12%) were formed by $^1O_2$-addition to the (*Z*)-2-pentenyl C,C-double bond of **12**[6])[7]).

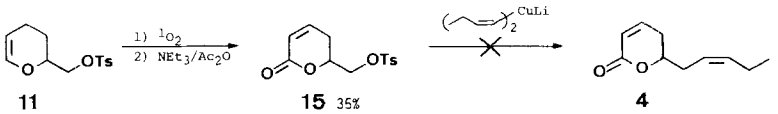
For the synthesis of jasmine lactone (**2**), acid-catalyzed addition of hydrogen peroxide on the enol ether double bond of **12** resulted in the exclusive formation

Scheme 4



5) Commercially available *(Degussa)*.
6) This lack of selectivity is discussed below.
7) No di-oxygenated products were isolated.

Scheme 5

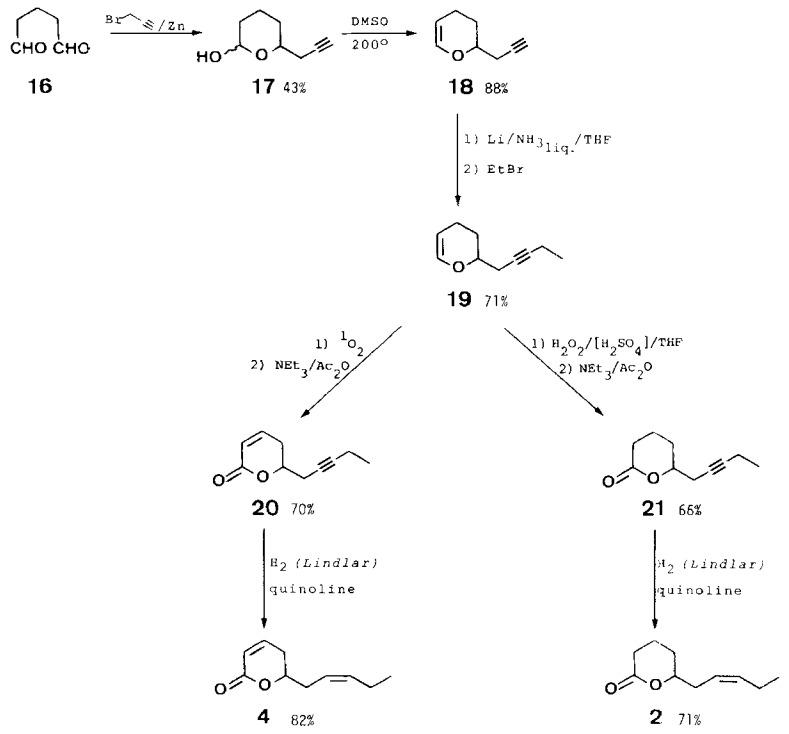


of the desired hydroperoxide, which was dehydrated to lactone **2** in 63% yield *(Scheme 4)*.

Alternative routes to tuberolactone (**4**). The low yield in the photooxygenation step **12** → **4** prompted us to reverse the reaction sequence *(Scheme 5)*. Lactone **15** was obtained from **11** in fair yield. But in an exploratory experiment, the reaction of **15** with lithium di((*Z*)-1-butenyl)cuprate, no tuberolactone (**4**) could be detected.

A further possibly improved way to **4** would be the photooxygenation of the acetylenic intermediate **19** which is expected to furnish lactone **20** selectively *(Scheme 6)*. After many unsuccessful attempts[8]) intermediate **19** became accessible

Scheme 6



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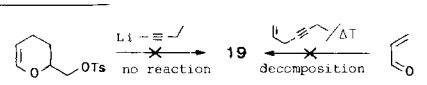
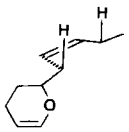
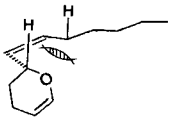
[8]) 

via mono-addition of (2-propynyl)zinc bromide to glutaraldehyde (**16**)[9]), followed by subsequent dehydration (→ **18**), metallation of the acetylene **18** and ethylation (overall yield 27%). Photooxygenation of **19** gave the expected lactone **20** as the sole product (70%). Catalytic hydrogenation finally afforded tuberolactone (**4**) in 82% yield.

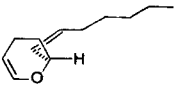
On the other hand, addition of hydrogen peroxide to **19** gave lactone **21**, which was hydrogenated to jasmine lactone (**2**; overall yield 47%).



12



10
disfavoured conformation

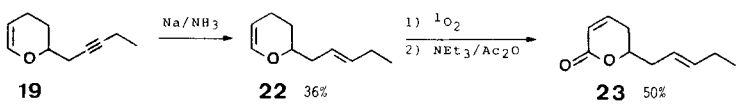


10
good conformation

Discussion. – The lack of selectivity of the photooxygenation of **12** to give tuberolactone (**4**; *Scheme 4*) is in contrast to the highly selective conversion of intermediate **10** into argentilactone (**5**; *Scheme 3*). The displacement of the C,C-double bond by one C-atom greatly influences its reactivity towards $^1O_2$. A possible explanation is that **12** has two allylic H-atoms in the side chain which can be perpendicular to the alkene plane. This is consistent with the observed *syn* preference in $^1O_2$-additions [13]. In contrast, the optimum conformation of **10** does not allow such a situation[10]).

Support for this hypothesis was provided by photooxygenation of 2-((*E*)-2-pentenyl)-3,4-dihydro-2*H*-pyran (**22**), easily obtained from **19** by reduction with sodium in ammonia *(Scheme 8)*. As expected $^1O_2$ added selectively to the dihydropyran double bond to afford **23** (the (*E*)-isomer of tuberolactone) in good yield.

Scheme 8



19 **22** 36% **23** 50%

We thank Drs. *K.H. Schulte-Elte, B. Maurer* and *R.L. Snowden*, Firmenich SA, for stimulating discussions and Mrs. *C. Grivet-Linder* and Mr. *C. Mazotti* for skillful technical assistance.

9) *Grignard* reaction following to a known procedure [12] gave predominantly di-addition products (in low yields).

10) It should be noted that other factors may influence the relative reactivities of **10** and **12**; for example, the inertness of the heptenyl side chain in **10** could be accounted for by the known reduced reactivity of allylic alcohols, hydroperoxides and ethers to $^1O_2$ [14].

Experimental Part

General. Each reaction was closely followed to completion by TLC. and GLC. (where necessary). Melting points are uncorrected. TLC. was performed using pre-coated plates (*Merck*, silica gel 60 F_{254}), Rf values being noted using an appropriate solvent; the spots were revealed by spraying with EtOH/anisaldehyde/H_2SO_4 18:1:1. GLC. were recorded on a *Carlo Erba Fractovap 2350*. The following spectrometers and solvents were used. IR.: *Perkin-Elmer A 21* or *Perkin-Elmer 157 G* spectrometer (films or $CDCl_3$ solutions; bands are given in cm^{-1}). ^{1}H-NMR.: *Varian A 60*, *Bruker H X 90/15*[11] and *WH 360 Bruker* ($CDCl_3$; chemical shifts are reported in ppm relative to tetramethylsilane (= 0 ppm) as internal standard, coupling constants are given in Hz and the multiplicities are abbreviated as follows: *s* = singlet, *d* = doublet, *t* = triplet, *'t'* = triplet-like multiplet, *qa* = quadruplet, *m* = multiplet). MS.: *Atlas CH*$_4$ (electron energy 70 eV). Abbreviations: PE = petroleum ether (30–50°), DMSO = dimethylsulfoxide, THF = tetrahydrofuran, aq. = aqueous, sat. = saturated.

1. *Synthesis of 2-pentyl-3,4-dihydro-2*H*-pyran* (**9**). A solution of acrolein (**6**; 28.6 g, 34.0 ml; 0.51 mol), 1-heptene (**8**; 200 g, 287.5 ml; 2.04 mol) and BHT (2,6-di-*t*-butyl-*p*-cresol; 3.0 g) was introduced, under N_2, into a steel-autoclave and heated for 25 h at 190°. Distillation of the yellow mixture gave 183.7 g of recovered **8**. The concentrated reaction mixture (37.6 g) was then distilled (bulb-to-bulb) at 60–100° (bath)/7 Torr. The product (16.4 g) was further purified by chromatography through silica gel (150 g) with cyclohexane/ethyl acetate 9:1. Pure **9** was obtained (12.8 g; 50% based on 16.3 g of reacted **8**). – IR. (neat): 3060, 2920, 2860, 1650, 1470, 1375, 1240, 1220, 1070, 1035. – ^{1}H-NMR. (60 MHz): 0.89 (*'t'*, $J \approx 6.0$, 3 H); 1.00–2.30 (*m*, 12 H); 3.80 (*m*, 1 H); 4.65 (*m*, 1 H); 6.35 (*d*, $J \approx 6.0$, 1 H). – MS.: 154 (55, M^+), 111 (13), 110 (14), 98 (56), 97 (28), 84 (17), 83 (63), 81 (26), 70 (67), 69 (45), 57 (97), 56 (59), 55 (100), 43 (34), 41 (65), 39 (37).

2. *Synthesis of massoia lactone* (**3**). Dihydropyran **9** (4.62 g; 30 mmol) and *meso*-tetraphenylporphine (200 mg; 0.32 mmol) were dissolved in toluene (80 ml) and introduced into a pyrex vessel, through which was bubbled pure O_2. The solution was irradiated with a high pressure mercury lamp (type *Philips*/125 W). After absorption of 560 ml (~0.87 mol-equiv.) of O_2 in 3½ h the solution was treated with triethylamine (2.61 g, 3.6 ml; 26.0 mmol) and acetic anhydride (3.91 g, 3.6 ml; 38.2 mmol), and stirred overnight at room temp. The mixture was extracted with ether, washed with water and sat. NaCl-solution, dried (N_2SO_4), and evaporated. The red oil (6.06 g) was distilled (bulb-to-bulb), b.p. 100–120° (bath)/0.05 Torr, to afford 3.56 g (71%) of 93% pure **3** (= 65% of pure **3**). For analytical purposes, a sample was purified by column chromatography (silica gel; cyclohexane/ethyl acetate 9:1). – IR. (neat): 2940, 1720, 1630, 1470, 1420, 1385, 1250, 1150, 1110, 1075, 1035. – ^{1}H-NMR. (60 MHz): 0.90 (*'t'*, $J \approx 6.0$, 3 H); 0.90–2.20 (*m*, 8 H); 2.34 (*m*, 2 H); 4.45 (*m*, 1 H); 5.98 (*d* × *t*, $J \approx 10.0$ and 2.0, 1 H); 6.87 (*d* × *t*, $J \approx 10.0$ and 4.0, 1 H). – MS.: 168 (trace, M^+), 108 (4), 97 (100), 68 (72), 55 (10), 43 (12), 41 (29).

3. *Synthesis of 2-((Z)-1-heptenyl)-3,4-dihydro-2*H*-pyran* (**10**). a) *Base system: NaH/DMSO.* NaH (55% dispersion in oil, 0.71 g; 16.2 mmol; 3 times washed with PE (5 ml)) was treated with DMSO (20 ml) and heated at 80° for 45 min. The solution was cooled to 20°, and hexyltriphenylphosphonium bromide (6.92 g; 16.2 mmol) [15] was added portionwise. The temp. rose to 35°, and a dark red slurry was formed. The mixture was stirred at 20° for 3 h, then acrolein dimer (**7**; 2.00 g; 17.8 mmol) was added dropwise. During the following exothermic reaction, the temp. was maintained (ice bath) at 35°. The pale brown mixture was stirred for 15 min, treated with PE and water, shaken and filtered. The collected triphenylphosphine oxide was thoroughly washed with PE, the filtrate extracted with water (4 times) and sat. NaCl-solution, dried (Na_2SO_4) and evaporated. Bulb-to-bulb distillation (100–140° (bath)/5 Torr) afforded 2.08 g (71%) of **10** (*Z*/*E* = 88:12). – IR. (neat): 3100, 2970, 1640, 1235, 1220, 1070, 1055, 1040. – ^{1}H-NMR. (60 MHz): 0.87 (*'t'*, $J \approx 6.0$, 3 H); *ca.* 1.00–2.30 (*m*, 12 H); 4.64 (*m*, 2 H); 5.51 (*m*, 2 H); 6.36 (*d*, $J \approx 6.0$, 1 H). – MS.: 180 (13, M^+), 124 (13), 109 (29), 95 (40), 81 (58), 68 (50), 67 (71), 54 (100), 41 (61).

b) *Base system:* $NaNH_2/NH_{3\,liq.}$. Hexyltriphenylphosphonium bromide (21.35 g; 50 mmol) was added portionwise to a stirred suspension of sodium amide (50.0 mmol) in liquid ammonia (250 ml) [16]. The orange mixture was stirred under reflux for 45 min, ammonia was evaporated and replaced by toluene (200 ml). The suspension was heated at 100° for 1 h, cooled at 20°, and filtered under N_2 using a *Schlenk* tube to remove NaBr. The dark red filtrate was added dropwise to an ice cooled solution of 7 (6.16 g; 55.0 mmol) in toluene (60 ml). After complete addition (90 min. exothermic reaction),

stirring was continued at 20° for 1 h. The usual work-up (*cf.* chapt. 3a) afforded 12.4 g of crude product. Bulb-to-bulb distillation gave 7.0 g (78%) of **10** (*Z*/*E* = 88:12).

c) *Base system: NaN(SiMe$_3$)$_2$/THF.* Hexyltriphenylphosphonium bromide (2.14 g, 5.0 mmol) was added portionwise to a solution of sodium 1,1,1,3,3,3-hexamethyl-1,3-disilazanide (1.01 g, 5.5 mmol) in THF (16 ml). The mixture was stirred at 20° for 30 min and under reflux for 1 h. The orange suspension was cooled to −78°, and **7** (0.61 g; 5.5 mmol) was added dropwise. After 1 h at −78°, stirring was continued at 20° for 1 h. Usual work-up (*cf.* 3a) and distillation afforded 484 mg (54%) of **10** (*Z*/*E* = 94:6).

4. *Synthesis of argentilactone* (**5**). Photooxygenation of **10** (*Z*/*E* = 94:6; 2.0 g; 11.1 mmol) as above gave 1.28 g (60%) of **5** (*Z*/*E* = 94:6) [4], b.p. 160° (bath)/0.02 Torr. – IR. (neat): 3050, 2945, 1735, 1470, 1420, 1405, 1240, 1150, 1055, 1025. – ^{1}H-NMR. (360 MHz): 0.89 (*t*, *J* ≈ 6.5, 3 H); 1.29 (*m*, 4 H); 1.39 (*m*, 2 H); 2.09 (*m*, 2 H); 2.34 (*d*×*d*×*d*, *J* ≈ 18.5, 5.5 and 5, 1 H); 2.43 (*d*×*d*×*d*×*d*, *J* ≈ 18.5, 11.0, 3.0 and 2.5, 1 H); 5.23 (*d*×*d*×*d*, *J* ≈ 11.0, 8.5 and 5.0, 1 H); 5.56 (*d*×*d*, *J* ≈ 10.5 and 8.5, 1 H); 5.66 (*d*×*t*, *J* ≈ 10.5 and 7.5, 1 H); 6.05 (*d*×*d*, *J* ≈ 10.0 and 2.5, 1 H); 6.89 (*d*×*d*×*d*, *J* ≈ 10.0, 5.5 and 3.0, 1 H). – MS.: 194 (7, M^+), 97 (20), 68 (100), 55 (15), 41 (25).

5. *Synthesis of (3,4-dihydro-2*H*-pyran-2-yl)methyl* p-*toluenesulfonate* (**11**). To a stirred suspension of $LiAlH_4$ (1.05 g; 27.5 mmol) in ether (30 ml) was added dropwise at 5–15° a solution of 7 (5.60 g; 50.0 mmol) in ether (20 ml). Then the mixture was stirred at 15° for 1 h, and carefully treated with water (1 ml), with 10% aq. NaOH-solution (1.5 ml) and again with water (2.5 ml). The white cake was filtered, and the filtrate evaporated (50°/12 Torr) and distilled to afford 5.30 g (93%) of (3,4-dihydro-2*H*-pyran-2-yl)methanol, b.p. 120° (bath)/8 Torr[11]).

A solution of (3,4-dihydro-2*H*-pyran-2-yl)methanol (5.0 g; 44.0 mmol) in pyridine (44 ml) was treated with tosyl chloride (12.6 g; 66.0 mmol). Then the reaction vessel was stoppered and stored in the refrigerator for 24 h. The mixture was poured onto ice, extracted with ether, the organic layer successively washed with water, cold 10% aq. HCl- and sat. aq. $NaHCO_3$-solution, water and sat. NaCl-solution, dried (Na_2SO_4) and evaporated. The solid product (11.7 g) was recrystallized (ether) to afford 11.0 g (93%) of **11**, m.p. 43–46°. – IR. ($CDCl_3$): 3150, 2950, 1650, 1605, 1450, 1360, 1270, 1190, 1165, 1060. – ^{1}H-NMR. (60 MHz): 1.50–2.15 (*m*, 4 H); 2.43 (*s*, 3 H); 4.09 (*m*, 3 H); 4.69 (*m*, 1 H); 6.24 (*d*, *J* ≈ 6.0, 1 H); 7.46 (*d*, *J* ≈ 8.0, 2 H); 7.78 (*d*, *J* ≈ 8.0, 2 H).

6. *Synthesis of 2-((*Z*)-2-pentenyl)-3,4-dihydro-2*H*-pyran* (**12**). *p*-Toluenesulfonate **11** (7.1 g; 26.5 mmol) in ether (30 ml) was added to a cooled (−60°) solution of lithium di((*Z*)-1-butenyl)cuprate (90.0 mmol) in ether (360 ml) [11]. The solution was stirred at −20 to −15° for 64 h. The mixture was quenched with sat. aq. NH_4Cl- and cold 10% aq. HCl-solution. The precipitate was removed by filtration. Extraction (ether) and successive washing with water, sat. aq. $NaHCO_3$-solution, water and sat. NaCl-solution afforded, after careful evaporation (20°/12 Torr), crude **12** (6.7 g, containing some ether). Bulb-to-bulb distillation gave at 50–80° (bath)/4 Torr 641 mg of 67% pure **12** (+ forerun) and at 80–100° (bath)/4 Torr 1.89 g of 90% pure **12**. Yield of **12**: 2.13 g (52%). – IR. ($CDCl_3$): 3150, 1650, 1245, 1225, 1065. – ^{1}H-NMR. (60 MHz): 0.99 (*t*, *J* ≈ 7.5, 3 H); 1.70–2.50 (*m*, 8 H); 4.82 (*m*, 1 H); 4.68 (*m*, 1 H); 5.47 (*m*, 2 H); 6.36 (*d*, *J* ≈ 6.0, 1 H). – MS.: 152 (12, M^+), 83 (100), 81 (20), 67 (15), 55 (39), 41 (23).

7. *Synthesis of tuberolactone* (**4**). Dihydropyran **12** (90% pure, 0.63 g; 3.37 mmol) and *meso*-tetraphenylporphine (50 mg; 0.08 mmol) in toluene (60 ml) were photooxygenated as above. Usual work-up and bulb-to-bulb distillation at 80–100° (bath)/0.01 Torr afforded a mixture of three isomers (93% pure, 382 mg; 58%): **4** (30%), **13** (16%), **14** (12%). Pure **4** (165 mg, 25%) was obtained by chromatography (silica gel, cyclohexane/ethyl acetate 9:1). – IR. ($CDCl_3$): 3025, 2975, 1720, 1380, 1260, 1150, 1050. – ^{1}H-NMR. (360 MHz): 1.00 (*t*, *J* ≈ 7.5, 3 H); 2.06 (*d*×*qa*, *J* ≈ 7.0 and 7.5, 2 H); 2.36 (*m*, 2 H); 2.50 (*m*, 2 H); 4.45 (*d*×*d*×*d*, *J* ≈ 11.0, 10.0 and 6.0, 1 H); 5.38 (*d*×*t*, *J* ≈ 11.0 and 7.0, 1 H); 5.58 (*d*×*t*, *J* ≈ 11.0 and 7.0, 1 H); 6.03 (*d*, *J* ≈ 10.0, 1 H); 6.88 (*d*×*d*×*d*, *J* ≈ 10.0, 5.0 and 4.0, 1 H). – MS.: 97 (100), 81 (18), 69 (31), 41 (44).

8. *Synthesis of 6-(*p*-toluenesulfonyloxymethyl)-5,6-dihydro-2(2*H*)-pyranone* (**15**). Photooxygenation of **11** (536 mg; 2.0 mmol) as above gave after the usual work-up 0.75 g of crude product, which was

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[11]) Also commercially available *(Degussa)*.

rapidly filtered on silica gel (ethyl acetate) and crystallized (ethyl acetate) to afford 200 mg (35%) of **15**. – IR. ($CDCl_3$): 2950, 1730, 1605, 1360, 1245. – ^{1}H-NMR. (60 MHz): 2.20–2.80 (*m*, 2 H and *s*, 3 H); 4.24 (*d*, $J \approx 4.0$, 2 H); 4.60 (*m*, 1 H); 6.00 (*d*, $J \approx 10.5$, 1 H); 6.90 (*d* × *t*, $J \approx 10.5$ and 4.5, 1 H); 7.39 (*d*, $J \approx 8.0$, 2 H); 7.82 (*d*, $J \approx 8.0$, 2 H).

9. *Synthesis of jasmine lactone* (**2**). A mixture of **12** (90% pure, 548 mg; 3.24 mmol), THF (10 ml), H_2O_2 (35%, 0.89 g; 9.2 mmol) and conc. H_2SO_4-solution (2 drops, 60 mg) was stirred at 20° for 24 h. The cloudy solution was poured into sat. aq. $(NH_4)_2SO_4$-solution, extracted (CH_2Cl_2), washed with sat. aq. $NaHCO_3$- and sat. NaCl-solution, dried (Na_2SO_4) and filtered. The filtrate was treated with triethylamine (0.28 g, 0.39 ml; 2.8 mmol) and acetic anhydride (0.42 g, 0.39 ml; 4.1 mmol), stirred at 20° for 2 h (→negative peroxide test), concentrated, diluted with ether/water 1:1, and stirred for 1 h (hydrolysis of excess acetic anhydride). Extraction and successive washing of the organic layer with 5% aq. HCl-, sat. aq. $NaHCO_3$- and sat. NaCl-solution afforded 555 mg of crude product. Bulb-to-bulb distillation gave at 100–110° (bath)/0.01 Torr 130 mg of 46% pure **2** and at 110–150° (bath)/0.01 Torr 300 mg of 95% pure **2**. Yield of **2**: 345 mg (63%). – IR. (neat): 3050, 2950, 1730, 1460, 1380, 1340, 1240, 1180, 1045, 940. – ^{1}H-NMR. (90 MHz): 0.98 (*t*, $J \approx 7.5$, 3 H); 1.60–2.80 (*m*, 10 H); 4.32 (*m*, 1 H); 5.50 (*m*, 2 H). – MS.: 168 (7, M^+), 152 (10), 131 (17), 116 (13), 101 (21), 99 (100), 83 (41), 81 (26), 71 (71), 55 (92), 43 (51), 41 (62).

10. *Synthesis of 6-(2-propynyl)-tetrahydropyran-2-ol* (**17**). Into a 250-ml-4-necked flask were introduced zinc chips (7.15 g; 110 mmol) which were covered with dry THF (25 ml). A portion of the 2-propynyl bromide (0.5 ml) was added at 20° under N_2. The mixture was heated at 50°, and after 1 min an exothermic reaction started (THF at reflux). The suspension was immediately cooled to −15° and the remainder of the 2-propynyl bromide (13.1 g; 110 mmol) in THF (15 ml) was added dropwise within 15 min, the temp. being maintained at 0–5°. Stirring mechanically and cooling at 0° were continued for 1 h. In another 250-ml-3-necked flask was placed a solution of glutaraldehyde (**16**)[12]) (16.5 g; 165 mmol) in THF (90 ml) under N_2. The fine grey suspension of (2-propynyl)zinc bromide was transferred under N_2 (*via* cannula) from the 1st flask into the dropping funnel of the 2nd flask and was added dropwise within 10 min to the water-cooled (10°) glutaraldehyde solution, reaction temp. 30–35° (for the reaction of (2-propynyl)zinc bromide with aldehydes s. [17]). The mixture was stirred for 1 h at 25°, hydrolyzed by the addition of sat. aq. NH_4Cl-solution and extracted (ethyl acetate). The resulting emulsion was filtered *(Celite)*, the organic layer was separated and washed with sat. NaCl-solution, dried (Na_2SO_4) and evaporated. The viscous residue (14.5 g)[13]) was purified by column chromatography[14]) on silica gel (80 g) with cyclohexane/ethyl acetate 4:1, yielding 7.30 g (43%) of 90% pure **17**[15])[16]). – IR. (neat): 3425, 3300, 2950, 2125, 1960[16]), 1440, 1200, 1020, 990. – ^{1}H-NMR. (60 MHz): 1.10–2.20 (*m*, 6 H, and at 2.03, *t*, $J \approx 2.5$, 1 H); 2.38 (*m*, 2 H); 3.40–4.40 (*m*, 2 H); 4.80 (*m*, 1 H). – MS.: 140 (2, M^+), 122 (7), 101 (56), 83 (41), 79 (37), 66 (35), 57 (100), 55 (58), 39 (49).

11. *Synthesis of 2-(2-propynyl)-3,4-dihydro-2*H*-pyran* (**18**). Hemiacetal **17** (7.30 g, 90% pure; 46.9 mmol) in DMSO (70 ml) was heated in a distillation apparatus at 200°. A mixture of **18**, DMSO and water distilled at 120–190°. It was treated with cold water and extracted with pentane (3 times). The pentane solution was washed successively with water and sat. NaCl-solution, dried (Na_2SO_4) and evaporated to afford **18** (5.11 g, 98% pure; 88%). – IR. ($CDCl_3$): 3300, 3075, 2925, 2850, 2125, 1960[16]), 1645, 1435, 1240, 1070. – ^{1}H-NMR. (60 MHz): 1.70–2.30 (*m*, 5 H); 2.30–2.60 (*m*, 2 H); 4.91 (*m*, 1 H); 4.80 (*m*, 1 H); 6.30 (*d*, $J \approx 7$, 1 H). – MS.: 122 (26, M^+), 93 (20), 83 (100), 79 (15), 66 (21), 55 (37), 39 (40).

12. *Synthesis of 2-(2-pentynyl)-3,4-dihydro-2*H*-pyran* (**19**). To a stirred suspension of lithium amide (38.0 mmol) in liquid ammonia (60 ml) [16] was added dropwise **18** (3.15 g, 98% pure; 25.3 mmol) in THF (4 ml). After 90 min the dark mixture was treated with a solution of bromoethane (4.20 g; 38.6 mmol) in THF (2 ml). The mixture (yellow-brown after 5 min) was stirred for 45 min and

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[12]) Preparation of anhydrous glutaraldehyde: [12].

[13]) GLC. analysis: 93% of **17** and 7% of 1,10-undecadiyne-4,8ξ-diol.

[14]) During an attempted distillation, a highly exothermic reaction led to polymerization (caution: *explosion*).

[15]) Mixture of diastereoisomers.

[16]) Contains 3% of isomeric allene.

diluted with THF (30 ml). Evaporation of ammonia, hydrolysis with sat. aq. NH_4Cl-solution (100 ml), extraction with ethyl acetate (3 times), washing of the extract with sat. NaCl-solution, drying (Na_2SO_4) and evaporation afforded a residue (4.4 g), which was distilled (bulb-to-bulb) at 120–150° (bath)/4 Torr to yield pure **19** (2.70 g, 71%). – IR. ($CDCl_3$): 3060, 2925, 2850, 1645, 1440, 1320, 1240, 1220, 1060. – ^{1}H-NMR. (60 MHz): 1.10 (*t*, $J \approx 7.5$, 3 H); 1.80–2.40 (*m*, 6 H); 2.30–2.60 (*m*, 2 H); 3.90 (*m*, 1 H); 4.80 (*m*, 1 H); 6.34 (*d*, $J \approx 6.5$). – MS.: 150 (10, M^+), 121 (25), 106 (8), 93 (13), 91 (18), 83 (100), 81 (21), 79 (28), 55 (40).

13. *Synthesis of 6-(2-pentynyl)-5,6-dihydro-2(2*H*)-pyranone* (**20**). Photooxygenation of **19** (1.00 g, 6.67 mmol) as above (**9**→**3**) using *meso*-tetraphenylporphine (100 mg, 0.16 mmol) in toluene (70 ml) (158 ml of O_2 in 4 h), followed by treatment with triethylamine (0.58 g, 0.8 ml; 5.8 mmol) and acetic anhydride (0.87 g, 0.8 ml; 8.5 mmol) gave 854 mg of **20** (90% pure; 70%), b.p. 110–150° (bath)/0.05 Torr. For characterization, a sample was redistilled. – IR. (neat): 2975, 2925, 1720, 1420, 1380, 1245, 1150, 1060. – ^{1}H-NMR. (60 MHz): 1.10 (*t*, $J \approx 7.5$, 3 H); 2.00–2.40 (*m*, 2 H); 2.30–2.80 (*m*, 4 H); 4.51 (*m*, 1 H); 6.03 (*d*×*t*, $J \approx 10.0$ and 2.0, 1 H); 6.93 (*d*×*t*, $J \approx 10.0$ and 4.0, 1 H). – MS.: 97 (100), 69 (26), 41 (41).

14. *Synthesis of tuberolactone* (**4**). Pyranone **20** (296 mg, 90% pure; 1.62 mmol) in hexane (15 ml) and quinoline (2 drops) was partially hydrogenated over *Lindlar* catalyst (5% Pd/C/$BaSO_4$; 100 mg). After absorption of 1 mol-equiv. of H_2 (43 ml), the suspension was filtered *(Celite)* and the residue was washed with cold 5% aq. HCl-solution. The aqueous layer was extracted with ether, and the combined organic layers were dried (Na_2SO_4) and evaporated. The crude product (305 mg) was distilled (bulb-to-bulb) at 110–150° (bath)/0.05 Torr to give pure **4**[17]), whose spectral data were identical to those reported above.

15. *Synthesis of 6-(2-pentynyl)-tetrahydro-2-pyranone* (**21**). A mixture of **19** (1.00 g; 6.67 mmol), THF (10 ml), H_2O_2 (35%, 1.29 g; 13.3 mmol) and conc. H_2SO_4-solution (2 drops) was stirred at 20° for 24 h. Work-up as above (**12**→**2**) afforded crude **21** (1.05 g). After bulb-to-bulb distillation (110–130° (bath)/0.01 Torr) 780 mg of **21** (93% pure; 66%) were obtained. – IR. (neat): 2950, 1730, 1440, 1380, 1320, 1240, 1180, 1050, 940. – ^{1}H-NMR. (60 MHz): 1.10 (*t*, $J \approx 7.5$, 3 H); 1.60–2.40 (*m*, 6 H); 2.30–2.80 (*m*, 4 H); 3.39 (*m*, 1 H). – MS.: 166 (trace, M^+), 99 (100), 71 (41), 55 (35), 43 (27), 41 (20).

16. *Synthesis of jasmine lactone* (**2**). Pyranone **21** (400 mg, 93% pure; 2.24 mmol) was hydrogenated as above (**20**→**4**) to give pure **2**[17]) (267 mg, 71%), b.p. 110–140° (bath)/0.01 Torr, whose spectral data were identical to those reported above.

17. *Synthesis of 2-((*E*)-2-pentenyl)-3,4-dihydro-2*H*-pyran* (**22**). Sodium chips (610 mg; 26.6 mmol) were added to liquid ammonia (60 ml, distilled over sodium). To the dark blue solution was rapidly added (*via* syringe) **19** (2.00 g, 13.3 mmol). The mixture became yellow, then red and was quenched with sat. aq. NH_4Cl-solution (5 ml) and ethyl acetate (20 ml). After evaporation of the residual ammonia, extraction, washing of the organic layer with sat. NaCl-solution, drying (Na_2SO_4), and evaporation of the solvent a residue was obtained (1.9 g), which was distilled to give pure **22** (735 mg, 36%)[18]). – IR. (neat): 3075, 2925, 1640, 1440, 1240, 1060, 970. – ^{1}H-NMR. (60 MHz): 0.97 (*t*, $J \approx 7.5$, 3 H); 1.60–2.50 (*m*, 8 H); 3.79 (*m*, 1 H); 4.66 (*m*, 1 H); 5.50 (*m*, 2 H); 6.34 (*d*, $J \approx 6.5$, 1 H). – MS.: (12, M^+), 95 (7), 83 (100), 81 (16), 67 (12), 55 (36), 41 (18).

18. *Synthesis of 6-((*E*)-2-pentenyl)-5,6-dihydro-2(2*H*)-pyranone* (**23**). Pyranone **22** (300 mg; 1.97 mmol) was photooxygenated as above (**9**→**3**) to give 310 mg of the (*E*)-isomer **23** of tuberolactone, b.p. 100–150° (bath)/0.05 Torr. After chromatography, 164 mg (50%) of pure **23** were obtained. – IR. ($CDCl_3$): 2975, 1720, 1390, 1250, 1045, 970. – ^{1}H-NMR. (60 MHz): 0.97 (*t*, $J \approx 7.5$, 3 H); 1.80–2.60 (*m*, 6 H); 4.43 (*m*, 1 H); 5.52 (*m*, 2 H); 6.00 (*d*×*t*, $J \approx 10.0$ and 2.0, 1 H); 6.89 (*d*×*t*, $J \approx 10.0$ and 4.0, 1 H). – MS.: 97 (100), 81 (6), 69 (27), 41 (34).

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[17]) Stereochemical purity > 96%. No trace of the (*E*)-isomer was detected.

[18]) Compound **22** partially decomposed during the distillation.

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